UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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In re:

REZULIN PRODUCTS LIABILITY LITIGATION
(MDL No. 1348)

MASTER FILE
00 Civ. 2843 (LAK)

This Document Relates to: 00 Civ. 9168, 00 Civ. 3098, 01 Civ. 6066, 01 Civ. 8171, 01 Civ. 11878, 02 Civ. 1719, 02 Civ. 8395, 03 Civ. 2861, 03 Civ. 2863, 03 Civ. 2864, 03 Civ. 2865, 03 Civ. 2867, 04 Civ. 4916, 04 Civ. 7807, 04 Civ. 8538, 04 Civ. 8539, 04 Civ. 8940, 04 Civ. 8941, 04 Civ. 8942.

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MEMORANDUM OPINION

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LEWIS A. KAPLAN, *District Judge*.

Defendants Pfizer, Inc., Warner-Lambert Company, and Parke-Davis (collectively, "Pfizer") move for an order excluding the proposed opinion testimony of experts in reports submitted by 28 plaintiffs[1] and granting summary judgment dismissing those plaintiffs' claims. Pfizer argues that the expert reports are not admissible.

I. Background and Undisputed Facts

A. Procedural History

These actions arise from the use of the prescription diabetes medication Rezulin, formerly manufactured by defendants Warner-Lambert Co. and its Parke-Davis division. The drug was approved by the Food and Drug Administration in 1997 but was withdrawn from the market in 2000 after reports that some patients taking it experienced liver failure[2] Thousands of lawsuits for alleged personal injuries ensued. The federal actions, including those at issue here, were

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[1] Pfizer's motion was filed against 30 plaintiffs. *See* Def. Mem. at 2. Thereafter, plaintiff Alarcon's case was dismissed voluntarily with prejudice and plaintiff Rattray's case was stayed pursuant to Pretrial Order ("PTO") No. 401 after he agreed to participate in the settlement program. *See* Def. Reply at 1 n.1.

[2] *See In re Rezulin Prod. Liab.*, 369 F. Supp. 2d 398, 400 (S.D.N.Y. 2005) (the "*Silent Injury*" decision).

consolidated before this Court for pre-trial proceedings by the Judicial Panel on Multidistrict Litigation.[3]

After extensive discovery, Pfizer moved pursuant to Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.,*[4] to exclude proposed expert testimony proffered by the Plaintiffs' Steering Committee ("PSC") to the effect that Rezulin can cause so-called silent injury to the liver – that is, that Rezulin can cause liver injury in the absence of marked elevation of specific liver enzymes while the patient was taking the drug.[5] In the *Silent Injury* opinion, familiarity with which is assumed, the Court analyzed the proposed expert testimony, which was intended to provide a basis for finding general causation,[6] and concluded that plaintiffs had not established the reliability of the silent injury theory:

> "The theory never has been tested or peer-reviewed, has not been published except by [one proposed expert] after the commencement of this litigation and only then in speculative terms and suspicious circumstances, and has no acceptance outside this litigation. The plaintiffs' experts have ignored information that appears to call

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3 *See In re Rezulin Prod. Liab. Litig.*, 361 F. Supp. 2d 268, 269 (S.D.N.Y. 2005) (the "*No Injury*" decision).

4 509 U.S. 579 (1993).

5 *See Silent Injury*, 369 F. Supp. 2d at 401. "Marked elevation of liver enzymes" was defined as an increase in the concentration of the blood of four specific substances to more than twice the upper limit of the normal range, while "while the patient was taking the medication" was defined as "up to fifteen days after the patient stopped taking Rezulin (for purposes of hepatocellular injury) and up to one month after the patient stopped taking Rezulin (for purposes of cholestatic or mixed injury)." *Id.* at 407, n.7.

6 To prevail in a toxic tort case, a plaintiff must demonstrate both general and specific causation. *See id.* at 401-02. "General causation is whether a substance is capable of causing a particular injury or condition in the general population, while specific causation is whether a substance caused a particular individual's injury." *Id.* at 402 (internal citations and quotations omitted).

> crucial aspects of their theory into question. The theory rests on a series of empirically unbridgeable analytical gaps. Most importantly, the experts have not established a sound basis for concluding that Rezulin-induced apoptosis can occur at clinically significant levels and remain silent. Similarly, the experts have failed to show that any mitochondrial changes attributable to Rezulin themselves can cause apoptosis or that any cholestatic injury due to Rezulin's effect on the BSEP would be silent.
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> ". . . The plaintiffs attempt to deal with all of these problems by arguing that the testimony in question could factor into the diagnosis of an individual patient. The plaintiffs' position is that a physician, faced with a patient who took Rezulin and had symptoms of liver disease but no elevated enzymes, could use the opinions of [plaintiffs' experts] and the research they cite to conclude that the patient's injury was caused by Rezulin. The flaw, however, is that a physician must have some reliable basis for believing that a particular substance is capable of causing the injury in question in relevant circumstances before concluding that the substance caused that injury in a particular case. Here, there is no such basis."[7]

The Court accordingly granted Pfizer's motion to exclude the proposed expert testimony on Rezulin's ability to cause silent liver injury.

The Court later issued a so-called *Lone Pine* order, which required each plaintiff to consider whether good grounds existed to continue prosecuting his or her claim in light of the *Silent Injury* and other decisions.[8] If a plaintiff concluded that good cause to continue existed, he or she was required to provide an expert report reflecting, among other things, "[w]hether the plaintiff's medical records report that the plaintiff had [specific liver enzyme] levels more than two times the

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[7] *Id.* at 438. This latter point was upheld by the Court of Appeals on an appeal from another order in this MDL. *See Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249, 252 n.1 (2d Cir. 2005).

[8] *See* Pretrial Order No. 370 at 2.

upper limit of normal range while the plaintiff was on Rezulin therapy or within 30 days after the last use of Rezulin" and an "expert's opinion on causation of each claimed injury."[9]

B. Plaintiffs' Lone Pine *Submissions*

All 28 plaintiffs whose complaints are the subject of this motion subsequently submitted expert opinions.[10] Although each opinion states that the given plaintiff sustained a liver injury attributable to Rezulin, no plaintiff has provided evidence that his or her liver enzyme levels were more than two times the upper limit of normal range while he or she was on Rezulin or within 30 days of ceasing the therapy.[11] Most of the plaintiffs rely on opinions from the same handful of

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9 *Id.* at 2-3.

10 For convenience, the 28 plaintiffs can be grouped according to their counsel. Plaintiff Anderson is represented by Berger & Zavesky Co., L.P.A. (the "Zavesky plaintiff"). Plaintiffs Hughes and Prince are represented jointly by Waite, Scheider, Bayless & Chesley Co., L.P.A. and Berger & Zavesky (the "Chesley plaintiffs"). The remaining 25 plaintiffs are represented by Littlepage Booth (the "Littlepage plaintiffs").

11 *See generally* Def. Rule 56.1 Statement; Littlepage Pl. Response to Rule 56.1 Statement; Chesley Pl. Response to Rule 56.1 Statement. As the Zavesky plaintiff did not respond to Pfizer's Rule 56.1 Statement, those facts relating to her, Undisputed Facts 2(a)-(c), are deemed admitted. *See*Local Rule 56.1; *see also In re Rezulin Prod. Liab. Litig.*, 2005 WL 254313, *2 (S.D.N.Y. Feb. 2, 2005). Thus she has admitted that her liver enzyme levels did not exceed two times the upper limit of normal during the relevant time period.

The Chesley plaintiffs expressly admit that their liver enzyme levels were not greater than two times the upper limit of normal during the relevant time period. *See* Chesley Pl. Response to Rule 56.1 Statement at 14(a)-(c), 20(a)-(c).

The Littlepage plaintiffs take a more veiled approach. For example, the response to Undisputed Fact 3(b), that plaintiff Borklund's liver enzyme test results indicate that the enzymes were not elevated more than two times the upper limit of normal range during the relevant time period, is that "[p]laintiff[']s liver enzyme elevations were not within normal limits." Littlepage Pl. Response to 56.1 Statement at 3(b). In response to Undisputed Fact 3(c), that there is no evidence that Borklund's liver enzyme levels were ever elevated to the

experts,[12] some of whom were already considered on the previous motion. Their opinions are summarized below.

1. Dr. Glenn Wilson, Ph.D.[13]

Dr. Wilson, a biomedical scientist[14] and professor at the University of South Alabama College of Medicine, opines that Rezulin can injure the mitochondria of cells with which it comes into contact.[15] He states that Rezulin reduces blood sugar levels by damaging mitochondria, which

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relevant range, she states that there is a genuine issue of material fact "as to whether an elevation of liver enzymes between 1 and 2 times the upper limits of normal while on Rezulin constitutes hepatocellular injury caused by Rezulin." *Id.* at 3(c). The responses of the remaining 24 Littlepage plaintiffs are identical. *See generally* Littlepage Pl. Response to Rule 56.1 Statement.

Local Rule 56.1 requires a responding party to specifically controvert the undisputed facts or suffer their admission. *See also No Injury*, 361 F. Supp. 2d at 270 n.7. The Littlepage plaintiffs' responses do not address the facts asserted, making them deficient under Local Rule 56.1. The factual statements set forth in Pfizer's Rule 56.1 Statement – that the Littlepage plaintiffs' test results do not indicate liver enzymes elevated more than two times the upper limit of normal range during the relevant time period, and that no other evidence so indicates – therefore are deemed admitted.

12 The Littlepage plaintiffs have withdrawn Dr. John Gueriguian as a general causation expert. *See* Littlepage Mem. at 19.

13 Dr. Wilson's expert report is relied upon by the Littlepage plaintiffs as a basis for general causation. Slonim Decl., ¶ 6.

14 Def. Reply, Ex. C (Mar. 9, 2006 Wilson Dep.) at 2-25.

15 *See* Slonim Decl., Ex. 4 (the "Wilson Report") at 25.

then results in "organ toxicity, dysfunction, and failure through apoptosis, necrosis, and impaired ATP (energy) production within the organ."[16]

In reaching this conclusion, Dr. Wilson relies on a variety of data, including drug class effect information, *in vitro* cell testing, *in vivo* animal testing, human clinical trials, and case reports.[17] He relies also on an *in vitro* study he performed on normal human hepatocytes exposed to Rezulin at concentrations of 5 and 50 μM, both with and without the presence of fetal bovine albumin.[18] This study found that Rezulin causes cell death in normal human hepatocytes *in vitro*, even in the presence of albumin, "at [Rezulin] concentrations comparable to those [allegedly] found in vivo in the patients taking Rezulin."[19] The mechanism for this toxicity, Dr. Wilson states, is damage to the mitochondria, manifested "as a significant reduction in cellular ATP [] at lower doses and cell death at higher doses."[20]

This study – which has not been published, subjected to peer review, or independently validated or duplicated – did not measure liver enzyme levels or the effect of Rezulin in living humans or animals.[21] It was prepared for this litigation and was funded at least in part by

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16 *Id.*

17 *See id.* at 26-27.

18 *See id.* at 31-32.

19 Wilson Report at 33.

20 *Id.*

21 *See* Def. Reply, Ex. C (Mar. 9, 2006 Wilson Dep.) at 153:12-154:1.

the Littlepage law firm.[22] Nor does the study address the potential concentration discrepancies discussed in the *Silent Injury* decision – whether the concentrations of troglitazone used in this and other studies match the concentrations of the drug to which the outside of the cells in patients actually were exposed – or the question of how troglitazone is distributed in the liver.[23]

Finally, Dr. Wilson does not state that Rezulin can cause silent injury to human hepatocytes, by apoptosis or otherwise.[24] The Littlepage plaintiffs' lawyers incorrectly suggest that he concludes that "[m]ost importantly, because Rezulin's mechanism of injury is directed at the cell's mitochondria and it causes apoptosis, most of this damage occurs without any easy diagnostic means of detection."[25] But Dr. Wilson's report makes no such statement and provides no basis for drawing such a conclusion.[26] Rather, he confines his conclusions to the medication's toxicity and mechanism of harming the cell and does not opine on what happens after the cell is harmed.[27]

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22 *See id.* at 92:7-93:22, 121-22.

23 *See* 369 F. Supp. 2d at 432-36.

24 *See generally* Wilson Report.

25 Littlepage Opp. at 27.

26 *See generally* Wilson Report.

27 *See generally id.*

2. Dr. Herbert A. Rubin, M.D.[28]

Dr. Rubin, a board-certified internist specializing in gastroenterology,[29] states that Rezulin is a known hepatotoxin causing "a multitude of hepatocellular injuries including, but not limited to, cytolytic hepatitis, steatosis, microvesicular steatosis, apoptosis, and cholestatis."[30] He bases his conclusions on internal Pfizer documents, the testimony of Pfizer employees and experts, other experts' testimony, his own experience as a clinician, and the published medical literature.[31] In analyzing the cause of the Littlepage plaintiffs' alleged symptoms, he states that the "damage Rezulin causes to liver cells leads to liver cell death via apoptosis. Cell death by apoptosis does not result in the release of [liver enzymes] into the blood stream unless there has been massive liver cell death."[32] He does not, however, provide any support for this conclusion about silent liver injury.[33]

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28 Dr. Rubin submitted an expert report as to general and specific causation on behalf of each of the Littlepage plaintiffs. *See* Slonim Decl. ¶ 8, Exs. 7-31.

29 *See, e.g.*, Slomin Decl. Ex. 7 ("Rubin Report (Borklund)") ¶ 1.

30 *See id.* ¶ 7.

31 *See id.* ¶ 5.

32 *See id.* ¶ 19. Dr. Rubin makes similar, sometimes identical statements in his other opinions for Littlepage plaintiffs. *See, e.g.*, Slomin Decl. Ex. 8 ¶ 22(b) (apoptosis "is usually biochemically silent and therefore most often not detectable by blood test unless and until there has been significant cell death within a short time period"); Ex. 9 ¶ 22(b) ("The resulting inflammatory reaction leads to further cell death which may itself be biochemically silent on a blood test."); Ex. 10 ¶ 22(b) (identical to Ex. 8 ¶ 19); Ex. 11 ¶ 24(d) (same).

33 *See* Rubin Report (Borklund) ¶ 19.

3. Dr. Martyn Smith, Ph.D[34]

Dr. Smith, a toxicologist, testified at length at the *Silent Injury* hearing as to his theory that Rezulin can cause apoptosis by either triggering "a cascade of chemical events in which the mitochondria cease functioning normally and release a protein into the cytoplasm that triggers apoptosis" or interfering with the functioning of the bile salt export pump, which leads "to the build-up of toxic bile salts in the cells [which] triggers apoptosis."[35] The Court analyzed his opinion and conclusions in the *Silent Injury* decision, eventually excluding the opinion as evidence that Rezulin can cause liver injury in the absence of marked elevations of liver enzymes while a patient was taking the medication.[36]

Dr. Smith seeks to avoid that holding via a one-paragraph supplemental declaration that informs the Court that an article he authored was accepted for publication in a toxicology journal in June 2003.[37] That information, however, was considered in the Court's analysis in *Silent Injury*.[38] The supplemental declaration thus contains no new information or material relating to Dr. Smith's theories regarding apoptosis.

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34 Dr. Smith submitted a supplement to his general causation expert report on behalf of each of the 25 Littlepage plaintiffs. *See* Slonim Decl. ¶ 4, Ex. 3. Nonetheless, the Littlepage plaintiffs do not discuss Dr. Smith in their opposition brief. *See generally* Littlepage Mem.

35 *Silent Injury*, 369 F. Supp. 2d at 408.

36 *See id.* at 438.

37 *See* Slonim Decl. Ex. 3 (Smith Supp. Expert Decl.).

38 *See* 369 F. Supp. 2d at 423 n.158 (citing to published article). The article is attached.

4. Dr. Neil Julie, M.D.[39]

Dr. Julie, a medical doctor certified in internal medicine and gastroenterology, is licensed to practice medicine in Maryland.[40] He was a witness at the *Silent Injury* hearing as a potential general causation expert and, as with all the silent injury general causation experts considered at that hearing, his opinion was held inadmissible under Rule 702.[41]

Dr. Julie's report states that he has "reviewed an extensive amount of the published and unpublished literature regarding Rezulin [] and Rezulin-induced liver disease" and personally has treated "five patients who experienced Rezulin hepatotoxicity."[42] He states that it is generally accepted that Rezulin "is a hepatotoxin capable of causing, and has caused in patients exposed to the drug, a spectrum of injuries which can include jaundice, acute liver failure, severe liver injury, end-state liver disease and death"[43] and that it can cause apoptosis.[44] Dr. Julie does not offer a general causation opinion relating to silent injury.[45] Instead, after setting out background on the drug, he goes on to discuss plaintiff Gable's medical history relating to her alleged liver problems

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39 Dr. Julie submitted a specific causation report for plaintiff Gable, one of the Littlepage plaintiffs. *See* Slonim Decl. Ex. 14 (the "Julie Expert Decl.").

40 *See id.* ¶ 1.

41 *See Silent Injury*, 369 F. Supp. 2d at 408-09, 438.

42 Julie Expert Decl. ¶ 2.

43 *Id.* ¶ 7(a).

44 *See id.* ¶ 7(d).

45 *See generally id.*

and to conclude, supposedly by ruling out "all other likely or reasonable causes," that Gable's cirrhosis was caused by Rezulin.[46]

5. *Dr. Charles L. Mendenhall, M.D., Ph.D.*[47]

Dr. Mendenhall, a medical doctor with two years of specialized training in hepatology, is a Professor Emeritus at the University of Cincinnati College of Medicine.[48] He states that the "diagnosis and treatment of injuries to the liver and liver disease have composed the major portion of my professional practice for the past 37 years."[49]

Dr. Mendenhall states, without providing supporting data, that Rezulin, used in the management of diabetes, was withdrawn from the market due to the "very high incidence of abnormal biochemical tests consistent with liver injury."[50] After reviewing the medical records relating to Rezulin use and liver dysfunction of both Chesley plaintiffs, he concludes that "[h]aving reviewed this material in light of my training and experience, utilizing methodology commonly relied upon by hepatologists, it is my opinion, to a reasonable degree of medical certainty, that

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46 *Id.* ¶¶ 26-28.

47 Dr. Mendenhall has submitted expert reports on specific causation on behalf of each of the Chesley plaintiffs. *See* Slonim Decl. Exs. 34 ("Mendenhall Expert Report (Hughes)"), 35 ("Mendenhall Expert Report (Prince)").

48 *See* Mendenhall Expert Report (Prince) ¶ 2.

49 *Id.* ¶ 6.

50 *Id.* ¶ 9.

Rezulin caused" each Chesley plaintiff's liver disease or injury.[51] Dr. Mendenhall does not opine as to whether Rezulin can cause silent liver injury or that it did so in the Chesley plaintiffs in particular.[52]

6. Dr. David A. Rigle, M.D.[53]

Dr. Rigle is a medical doctor certified in forensic medicine. His report details the Zavesky plaintiff's medical history relating to liver and Rezulin issues, noting that the results of liver enzyme studies were either unavailable or normal.[54] After referring to the plaintiff's death from cirrhosis, Dr. Rigle opines that Rezulin "was a significant contributing causative factor in her development of liver failure and her eventual demise."[55] He bases this conclusion on the failure of her clinicians to arrive at an alternative diagnosis and on the consistency of her symptoms with those seen in Rezulin toxicity.[56] He states that "Rezulin is found to place in motion the pathologic changes that lead to cirrhosis and death early on during the course of treatment and there may be only a mild

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51 *Id.* ¶ 15; Mendenhall Expert Report (Hughes) ¶ 14.

52 *See generally* Mendenhall Expert Report (Prince); Mendenhall Expert Report (Hughes).

53 Dr. Rigle submitted a general and specific causation report on behalf of the Zavesky plaintiff. *See* Slonim Decl. Ex. 33 ("Rigle Expert Report").

54 *See id.* pp. 2-4.

55 *Id.* p. 3.

56 *See id.*

increase in liver enzymes observed,"[57] but provides no support for this conclusion about silent liver injury.

II. Legal Standard

A. Summary Judgment

Summary judgment is appropriate if there is no genuine issue of material fact and the moving party is entitled to judgment as a matter of law.[58] The moving party has the burden of demonstrating the absence of a genuine issue of material fact,[59] and the Court must view the facts in the light most favorable to the nonmoving party.[60] Where the burden of proof at trial would fall on the nonmoving party, it ordinarily is sufficient for the movant to point to a lack of evidence to go to the trier of fact on an essential element of the nonmovant's claim.[61] In that event, the

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57 *Id.* p. 4.

58 FED. R. CIV. P. 56(c); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986); *White v. ABCO Eng'g Corp.*, 221 F.3d 293, 300 (2d Cir. 2000).

59 *Adickes v. S.H. Kress & Co.*, 398 U.S. 144, 157 (1970).

60 *United States v. Diebold, Inc.*, 369 U.S. 654, 655 (1962); *Hetchkop v. Woodlawn at Grassmere, Inc.*, 116 F.3d 28, 33 (2d Cir. 1997).

61 *Celotex Corp. v. Catrett*, 477 U.S. 317, 322-23 (1986); *Virgin Atl. Airways Ltd. v. British Airways Plc*, 257 F.3d 256, 273 (2d Cir. 2001).

nonmoving party must come forward with admissible evidence[62] sufficient to raise a genuine issue of fact for trial.[63]

B. Causation

In a product liability case such as these, a plaintiff must prove both general and specific causation as part of his or her *prima facie* case.[64] General causation "bears on whether *the type of injury at issue can be caused or exacerbated* by the defendant's product," while specific causation addresses "whether, in the particular instance, the injury *actually was caused or exacerbated* by the defendant's product."[65] Further, proof of general causation is a necessary predicate for that of specific causation – if there is no evidence that a product is capable of causing the kind of harm claimed, then there is no basis to accept evidence that the product in fact did so in a specific case.[66]

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62 *See, e.g.*, *Nora Beverages, Inc. v. Perrier Group of Am., Inc*., 269 F.3d 114, 123-24 (2d Cir. 2001).

63 *See, e.g.*, *Nebraska v. Wyoming*, 507 U.S. 584, 590 (1993); *Goenaga v. March of Dimes Birth Defects Found.*, 51 F.3d 14, 18 (2d Cir. 1995).

64 *Ruggiero,* 424 F.3d at 252 n.1; *see also Silent Injury*, 369 F. Supp. 2d at 401-02.

65 *Id.* (emphasis in original); *see also Silent Injury*, 369 F. Supp. 2d at 402 ("General causation is established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance can cause a particular disease (e.g., that smoking cigarettes can cause lung cancer). Specific, or individual, causation, however, is established by demonstrating that a given exposure is the cause of an individual's disease (e.g., that a specific plaintiff's lung cancer was caused by his smoking).") (internal citations and quotations omitted).

66 *See id.*

The plaintiffs here do not contest that they must prove both kinds of causation through expert, not lay, testimony.[67] This is a requirement in every state in which these plaintiffs have brought their claims.[68]

III. The Proffered Expert Testimony

As the Court set out in its *Silent Injury* opinion,[69] the admission of scientific or other expert testimony is governed by Federal Rule of Evidence 702:

> "If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an

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67 *See, e.g., Wills v. Amerada Hess Corp.*, 379 F.3d 32, 46 (2d Cir. 2004) ("[W]here an injury has multiple potential etiologies, expert testimony is necessary to establish causation").

68 *See, e.g., Rink v. Cheminova, Inc.*, 400 F.3d 1286, 1295-96 (11th Cir. 2005) (applying Florida law) (affirming summary judgment in favor of defendant because without expert testimony, "proof that defective Fyfanon caused the injuries alleged by the putative class representatives was lacking"); *Emody v. Medtronic, Inc.*, 238 F. Supp. 2d 1291, 1295 *N.D. Ala. 2003) (applying Alabama law) (granting summary judgment in favor of defendant since "[a]n essential element of all product liability cases is expert testimony, passing Daubert muster, that a defect was the medical cause of plaintiff's claimed injuries") (internal citations omitted); *Valentine v. PPG Indus., Inc.*, 821 N.E.2d 580, 588, 158 Ohio App.3d 615, 623 (Ohio Ct. App. 2004) (affirming summary judgment in favor of defendant because "[t]o prove the proximate cause of a medical condition, here, a brain tumor, expert medical testimony ordinarily is necessary"); *Sanchez v. Saturn Corp.*, 2004 Tenn. LEXIS 711, *6-*8 (Tenn. Aug. 31, 2004) (affirming judgment that plaintiff failed to establish causation due to absence of expert testimony as "[p]roof of causation requires expert testimony in all but the most obvious cases"); *Christian v. Gray*, 65 P.3d 591, 601-02 (Okla. 2003) ("When an injury is of a nature requiring a skilled and professional person to determine cause and the extent thereof, the scientific question presented must necessarily be determined by testimony of skilled and professional persons.") (internal quotations omitted); *Wilhelm v. State Traffic Safety Commission*, 230 Md. 91, 185 A.2d 715 (1962) (expert testimony required to establish causal nexus between injury and effect); *Burroughs Wellcome Co. v. Crye*, 907 S.W.2d 497, 499, 38 Tex. Sup. Ct. J. 848, 850 (Tex. 1995) (reversing judgment in favor of plaintiff because "[t]he nature of a frostbite injury is such that expert medical testimony is required to establish causation").

69 369 F. Supp. 2d at 419.

> expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case."

The district court acts as a gatekeeper to ensure that "scientific testimony or evidence admitted is not only relevant, but reliable."[70] In other words, the court determines whether the proposed expert will testify as to scientific knowledge that

> "will assist the trier of fact to understand or determine a fact in issue. This entails a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue."[71]

In conducting this "flexible" inquiry, a court may consider various factors, such as whether the expert's theory "can be (and has been) tested," whether it "has been subjected to peer review and publication," its "known or potential rate of error," and whether it has "widespread acceptance."[72]

Further, to meet Rule 702's requirements, the proffered testimony must "fit" the factual dispute at issue – in other words, it must be "sufficiently tied to the facts of the case that it will aid the jury in resolving a factual dispute."[73] As the Court stated in the *Silent Injury* decision, "[a] district court therefore is not required to admit opinion evidence that is connected to existing

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70 *Daubert,* 509 U.S. at 591.

71 *Id.* at 592-93.

72 *Id.* at 593-94. Other factors that courts consider include whether the opinion was developed for litigation and whether the expert has accounted adequately for obvious alternative explanations. *See Silent Injury*, 369 F. Supp. 2d at 420.

73 *Daubert*, 509 U.S. at 591.

data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered."[74]

Against this background, the Court turns to the admissibility of the proffered testimony of these six experts.

A. Dr. Wilson

The overwhelming majority of Dr. Wilson's report discusses the toxicity of Rezulin and its potentially harmful effects on liver tissue. But the present question is not whether the report is admissible evidence that Rezulin is a hepatotoxin. Most pharmaceuticals are hepatotoxic in some circumstances.[75] Instead, the issue is whether Dr. Wilson's report is admissible evidence that Rezulin is capable of causing and in fact caused the Littlepage plaintiffs' particular liver injuries.

Dr. Wilson's report details one new *in vitro* study on Rezulin's toxicity, which examined normal human hepatocytes exposed to Rezulin at concentrations of 5 and 50 μM, both with and without the presence of fetal bovine albumin.[76] This study thus may address some of the potential weaknesses in prior studies identified by the Court in the *Silent Injury* decision, such as the use of abnormal, non-human, or other tissue cells and the absence of albumin.[77] It did not, however, address the potential problems previously identified with prior studies' concentration

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74 *Silent Injury*, 369 F. Supp. 2d at 420 (internal citations and quotations omitted).

75 *Silent Injury*, 369 F. Supp. 2d at 405.

76 *See* Wilson Report at 31-32.

77 *See* 369 F. Supp. 2d at 428-431.

discrepancies and liver distribution issues.[78] Further, the study has not been published or independently validated[79] and is a product of this litigation.[80]

Ultimately, however, the Court need not decide whether this new study is reliable, because it does not relate to the issue here – whether there is a reliable basis for Dr. Wilson's opinion that Rezulin is capable of causing and in fact caused the Littlepage plaintiffs' particular liver injuries. Dr. Wilson did not measure liver enzyme levels or the effect of Rezulin in living humans or animals in this new study or, indeed, at any time. Contrary to the Littlepage plaintiffs' assertions, his opinion does not state that Rezulin can cause silent injury to human hepatocytes by apoptosis or otherwise.[81] The report therefore does not raise a genuine issue of material fact as to general or specific causation of silent liver injury.

B. Dr. Rubin

Unlike Dr. Wilson's report, Dr. Rubin's report does attempt to draw a conclusion as to silent injury causation. The report asserts that "[c]ell death by apoptosis does not result in the release of [liver enzymes] into the blood stream unless there has been massive liver cell death."[82]

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78 *See id.* at 432-36.

79 *See* Def. Reply, Ex. C (Mar. 9, 2006 Wilson Dep.) at 153-154.

80 *See id.* at 92-93, 121-22.

81 *See generally* Wilson Report.

82 *See, e.g.,* Rubin Report (Borklund) ¶ 19.

However, it provides no support for this conclusion.[83] Without that support, the opinion is identical to those rejected as inadmissible in the *Silent Injury* analysis. It accordingly is not admissible evidence of general or specific causation.

C. Dr. Smith

Dr. Smith's supplemental declaration informs the Court that an article that he authored was accepted for publication in a toxicology journal in June 2003.[84] This article and its publication were considered in the Court's analysis in *Silent Injury*.[85] The supplemental declaration thus contains no new information or material relating to Dr. Smith's theories regarding apoptosis and is not admissible evidence as to general or specific causation. There is no reason to alter the prior conclusion as to the admissibility of his opinion.

D. Dr. Julie

Dr. Julie's specific causation opinion for plaintiff Gable also is inadmissible. In the first instance, evidence of specific causation is irrelevant without evidence of general causation.[86] Dr. Julie nowhere offers any opinion as to general causation of silent liver injury.[87] Moreover, his

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83 *See id*.

84 *See* Slonim Decl. Ex. 3 (Smith Supp. Expert Decl.).

85 *See* 369 F. Supp. 2d at 423 n.158 (citing to published article).

86 *See, e.g., Ruggiero,* 424 F.3d at 252 n.1.

87 *See* Julie Expert Decl., ¶¶ 26-28.

differential diagnosis approach was rejected in the *Silent Injury* decision as a substitute for general causation.[88] That conclusion has been affirmed by the Second Circuit.[89] Accordingly, Dr. Julie's report is inadmissible.

E. Dr. Mendenhall

Nor does Dr. Mendenhall's report state any opinion as to general causation.[90] His specific causation analysis thus is without foundation.[91] In addition, like Dr. Wilson, he offers no opinion as to whether Rezulin can cause liver injury without marked elevation of liver enzymes.[92] His opinion therefore is inadmissible.

F. Dr. Rigle

This report suffers from the same deficiencies as do those of Drs. Rubin and Mendenhall. Although Dr. Rigle states that "only a mild increase in liver enzymes [may be] observed" when Rezulin causes liver injury,[93] he provides no support for this conclusion. It therefore is inadmissible under the *Silent Injury* decision, as is his differential diagnosis of the

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88 *See* 361 F. Supp. 2d at 435-438.

89 *See Ruggiero*, 424 F.3d at 254.

90 *See generally* Mendenhall Expert Report (Prince); Mendenhall Expert Report (Hughes).

91 *See, e.g., Ruggiero,* 424 F.3d at 252 n.1.

92 *See generally* Mendenhall Expert Report (Prince); Mendenhall Expert Report (Hughes).

93 *See* Rigle Report, p. 4.

specific cause of the Zavesky plaintiff's liver injury.[94] The report therefore is inadmissible as evidence of causation.

G. Application to Plaintiffs

1. The Littlepage Plaintiffs

To reiterate, the 25 Littlepage plaintiffs have provided no evidence that any of their liver enzyme levels was more than two times the upper limit of normal range while they were on Rezulin or within 30 days of ceasing the therapy.[95] Since they have no evidence that their liver enzyme levels were elevated more than two times the upper limit of normal range while they were taking the medication, they necessarily are relying on the theory that Rezulin can cause liver injury without such enzyme level elevation.

All of the Littlepage plaintiffs rely on the opinions of Drs. Wilson and Rubin and the supplement to Dr. Smith's report. Plaintiff Gable relies also on the report of Dr. Julie. As these expert reports all are inadmissible as evidence of general or specific causation, the Littlepage plaintiffs have failed to come forward with admissible evidence showing a genuine issue of material fact as to causation.

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94 *See* 361 F. Supp. 2d at 435-438; *see also Ruggiero*, 424 F.3d at 254.

95 *See generally* Def. Rule 56.1 Statement; Littlepage Pl. Response to Rule 56.1 Statement.

2. The Chesley Plaintiffs

Both Chesley plaintiffs admit that their liver enzyme levels were not greater than two times the upper limit of normal during the relevant time period.[96] They rely entirely on a silent injury theory of causation. Each offers only the expert report of Dr. Mendenhall as to specific causation. That report is not admissible evidence of causation. Accordingly, the Chesley plaintiffs also have failed to present admissible evidence demonstrating a genuine issue of material fact as to causation.

3. The Zavesky Plaintiff

The Zavesky plaintiff is deemed to have admitted that her liver enzyme levels did not exceed two times the upper limit of normal during the relevant time period.[97] She too therefore relies on a silent injury theory and offers only Dr. Rigle's expert report to establish specific causation. As Dr. Rigle's report is inadmissible, the Zavesky plaintiff has failed to offer admissible evidence showing the existence of a genuine issue of material fact as to causation.

IV. Conclusion

All 28 plaintiffs therefore have failed to provide admissible evidence of general or

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[96] *See* Chesley Pl. Response to Rule 56.1 Statement at 14(a)-(c), 20(a)-(c).

[97] *See generally* Def. Rule 56.1 Statement, Undisputed Facts 2(a)-(c); Local Rule 56.1.

specific causation of silent liver injury. Without the necessary and admissible expert evidence, there is no genuine issue of material fact as to causation, and summary judgment is appropriate.[98]

Pfizer's motion for summary judgment is granted[99] and the specific plaintiffs' complaints in the cases listed in the caption are dismissed.

SO ORDERED.

Dated: July 26, 2006

Lewis A. Kaplan
United States District Judge

(The manuscript signature above is not an image of the signature on the original document in the Court file.)

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98 *See* FED. R. CIV. P. 56(c); *Anderson,* 477 U.S. at 248.

99 Docket item 3694.